Predictive parameters for weaning from mechanical ventilation*

Parâmetros preditivos para o desmame da ventilação mecânica

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Abstract

The use of predictive parameters for weaning from mechanical ventilation is a rather polemic topic, and the results of studies on this topic are divergent. Regardless of the use of these predictive parameters, the spontaneous breathing trial (SBT) is recommended. The objective of the present study was to review the utility of predictive parameters for weaning in adults. To that end, we searched the Medline, LILACS, and PubMed databases in order to review articles published between 1991 and 2009, in English or in Portuguese, using the following search terms: weaning/*desmame*, extubation/*extubação*, and weaning indexes/*índices de desmame*. The use of clinical impression is an inexact means of predicting weaning outcomes. The most widely used weaning parameter is the RR/tidal volume (V_T) ratio, although this parameter presents heterogeneous results in terms of accuracy. Other relevant parameters are MIP, airway occlusion pressure ($P_{0.1}$), the $P_{0.1}$/MIP ratio, RR, V_T, minute volume, and the index based on compliance, RR, oxygenation, and MIP. An index created in Brazil, the integrative weaning index, has shown high accuracy. Although recommended, the SBT is inaccurate, approximately 15% of extubation failures going unidentified in SBTs. The main limitations of the weaning indexes are related to their use in specific populations, the cut-off points selected, and variations in the types of measurement. Since the SBT and the clinical impression are not 100% accurate, the weaning parameters can be useful, especially in situations in which the decision as to weaning is difficult.

Keywords: Weaning; Intensive care units; Ventilators, mechanical; Respiration, artificial.

Resumo

A utilização de parâmetros preditivos para o desmame da ventilação mecânica é um tema de grande polêmica, com estudos divergindo sobre esse assunto. Independentemente da utilização desses parâmetros preditivos, o teste de respiração espontânea (TRE) é recomendado. O objetivo do presente estudo foi revisar a utilidade dos parâmetros preditivos para o desmame em adultos. Para tanto, foram pesquisadas as bases de dados Medline, LILACS e PubMed e foram selecionados artigos publicados entre 1991 e 2009, em língua inglesa ou portuguesa, utilizando-se os seguintes termos: *weaning*/desmame; *extubation*/extubação e *weaning indexes*/índices de desmame. A utilização da impressão clínica é uma forma inexata para predizer o desfecho do desmame. O parâmetro mais utilizado é a relação FR/volume corrente (V_T), embora essa apresente resultados heterogêneos em termos de acurácia. Outros parâmetros relevantes são PImáx, pressão de oclusão nas vias aéreas ($P_{0,1}$), relação $P_{0,1}$/PImáx, FR, V_T, volume minuto e o índice composto por complacência, FR, oxigenação e PImáx. Criado no Brasil, o índice integrativo de desmame tem mostrado alta acurácia. Embora recomendado, o TRE não é acurado, não identificando aproximadamente 15% das falhas de extubação. As principais limitações dos índices de desmame são devidas ao seu uso em populações específicas, aos pontos de cortes selecionados e a variações nas formas de mensuração. Como o TRE e a impressão clínica não têm 100% de acurácia, os parâmetros de desmame podem ser úteis, principalmente em situações nas quais o processo de decisão para o desmame é difícil.

Descritores: Desmame; Unidades de terapia intensiva; Ventiladores mecânicos; Respiração artificial.

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Introduction

Although weaning from mechanical ventilation (MV) is successful in most cases, the first attempt fails in 20% of patients.[1] In addition, weaning accounts for over 40% of the total MV time,[1] the proportion varying in function of the etiology of respiratory failure. Prolonged MV is associated with various complications, such as ventilator-associated pneumonia,[2] ventilator-induced diaphragmatic dysfunction,[3,4] and critical illness polyneuropathy.[5] Therefore, in order to avoid these and other complications, patients should be weaned from MV as soon as possible. There are various weaning indices, all having the objective of establishing the prognosis for this process, which, contrary to what many think, cannot be established by clinical impression and the spontaneous breathing trial (SBT) alone.[6] Therefore, clinical impression in combination with an evaluation of the weaning indices and the SBT might provide a more precise prognosis for weaning from MV. The weaning indices are used in many ICUs, and various review articles have either recommended or have not ruled out the use of these indices.[1,6-11] Some of the most well-known weaning indices, such as the RR/tidal volume (V_T) ratio and MIP, have been incorporated into the routine of many ICUs and are measured prior to extubation. However, few of these indices have high accuracy,[12] and one study recommended that they not be used.[13] The objective of the present study was to review the utility of the weaning indices in adults being treated in a general ICU, with a focus on the most widely used and most accurate indices.

Research strategy

The present review was carried out by searching the Medline, LILACS, and PubMed databases in order to review articles published between 1991 and 2009, in English or in Portuguese, using the following search terms: weaning/*desmame*, extubation/*extubação*, and weaning indexes/*índices de desmame* (in intubated adults). We selected the reviews that were based on evidence or consensuses and those of greatest relevance, as well as the original articles of greatest impact, which had been cited in the reviews selected. We rejected articles that focused more on comparing modalities of MV weaning than on the weaning indices per se.

Essential definitions

Prolonged MV is defined as MV for more than 21 days and for more than 6 h/day.[10] The process of release from ventilatory support is defined as weaning from MV.[6] The SBT is the evaluation of tolerance to spontaneous breathing, for a period of 30 min to 2 h, on pressure support ventilation (PSV) at 7 cmH_2O, on continuous positive airway pressure (CPAP), or unassisted through a T-tube.[6] It is recommended that the SBT be performed prior to extubation.[7,8]

Successful weaning from MV is defined as spontaneous breathing (not requiring reintubation/MV) for at least the first 48 h after extubation.[8] A distinction is made between weaning failure (intolerance to the SBT without ventilatory support) and extubation failure (intolerance to extubation).[14]

A weaning index or predictive parameter for weaning is a criterion that evaluates a given physiological aspect of respiratory function, with the objective of distinguishing between patients who might tolerate the SBT and those who might not.[15] The weaning indices should be evaluated before the SBT, which functions as a diagnostic test to determine the probability of successful extubation.[8] Integrative parameters are those that evaluate more than one physiological aspect of respiratory function.

How can the accuracy of the predictive parameters for MV weaning be evaluated?

The diagnostic tests that are most widely used to evaluate the accuracy of the parameters for weaning from MV are as follows: sensitivity; specificity; positive predictive value (PPV); negative predictive value (NPV); positive likelihood ratio (PLR); negative likelihood ratio (NLR); post-test probability of weaning success or failure, determined by application of Bayes' theorem[13,16-18]; and calculation of the area under the curve (AUC) of the ROC curve, which is the test that is most widely used.[2,13,17-19]

In the context of MV weaning, the sensitivity of a measure is defined as its ability to accurately identify, from among the patients who present with a positive index (e.g., a RR/V_T ratio < 105

Chart 1 – Diagnostic tests available to evaluate the accuracy of the predictive parameters for weaning from mechanical ventilation.

Test	Formula
Sensitivity	*TP/(TP + FN) = frequency of TP = [1 – frequency of FN]*
Specificity	*TN/(TN + FP) = frequency of TN = [1 – frequency of FP]*
PPV	*TP/(TP + FP)*
NPV	*TN/(TN + FN)*
PLR	*Frequency of TP/frequency of FP = sensitivity/(1 – specificity)*
NLR	*Frequency of FN/frequency of TN = (1 – sensitivity)/specificity*

TP: true-positive; TN: true-negative; FP: false-positive; FN: false-negative; PLR: positive likelihood ratio; and NLR: negative likelihood ratio. Adapted from various sources.[13,15-19]

breaths • min^{-1} • L^{-1}), the proportion of those in whom weaning will be successful.[16] Conversely, the specificity of a measure is defined as its ability to identify, from among the patients who present with a negative index (e.g., a RR/V_T ratio > 105 breaths • min^{-1} • L^{-1}), the proportion of those in whom weaning will fail.[16] The PPV indicates the proportion of patients who present with a positive results for a given index and are successfully weaned from MV, whereas the NPV indicates the proportion of patients who present with negative results for a given index and fail in being weaned from MV.[16]

A true-positive test result correctly predicts successful MV weaning.[13,16] A true-negative test result correctly predicts unsuccessful MV weaning.[13,16] A false-positive test result predicts successful MV weaning, but the patient is not weaned from MV.[13,16] A false-negative test result predicts unsuccessful MV weaning, but the patient is weaned from MV.[13,16]

The PLR indicates the probability of a positive index resulting in successful weaning from MV, divided by the probability of the same index resulting in weaning failure.[16] In other words, the PLR expresses how many times it is more likely to obtain a positive result for a given index in patients who have been weaned from MV compared with those who have not.[16] The NLR indicates the probability of a negative index resulting in successful weaning from MV divided by the probability of the same index resulting in weaning failure.[16] In other words, the NLR expresses how many times it is more likely to obtain a negative result for a given index in patients who have not been weaned from MV compared with those who have.[16] An LR of 0.5-2.0 indicates that a parameter is mildly associated with the post-test probability of weaning success or failure. Values of LR of 2.0-5.0 and 0.3-0.5 are weakly but significantly associated with changes in the probability of weaning success or failure, respectively. Values of LR of 5.0-10.0 and 0.1-0.3 are more significantly associated with changes in the probability of weaning success or failure, respectively. Values of LR above 10 and below 0.1 are strongly associated with changes in the probability of weaning success or failure, respectively.[13] Chart 1 shows the diagnostic tests available, together with their respective formulas.

Bayes' theorem describes the relationship between pre- and post-test probability.[13,16] Therefore, Bayes' theorem evaluates the ability of an index to predict MV weaning outcome.[13,16]

The analysis of the ROC curve allows the ability of an index to discriminate between two groups of patients (those who have been weaned and those who have not) to be evaluated, with the advantage of not depending on the cut-off value selected.[13,16] According to one author,[20] based on the AUC, a test can be classified as follows: AUC < 0.50, uninformative; AUC of 0.50-0.69, inaccurate; AUC of 0.70-0.89, moderately accurate; AUC of 0.90-0.99, highly accurate; and AUC of 1.00, perfect.

Initiation of weaning from MV: clinical evaluation and predictive parameters

Patients can be weaned from MV if they meet at the following minimal criteria: resolution or stabilization of the underlying disease; adequate gas exchange; hemodynamic stability; and capacity to breathe spontaneously.[21] If these criteria are met, the SBT should be performed.

[1,7,8] If the clinical evaluation is unfavorable, the weaning indices are useless.[22] There is no sense in measuring the predictive parameters for weaning from MV if the condition that prompted the initiation of MV has not improved. However, when the clinical evaluation is favorable and the indices indicate a positive prognosis, the chances of success are greater.[22] Clinical evaluation in isolation does not accurately predict the outcome of weaning from MV,[6,10] the PPV and NPV of such evaluation being only 50% and 67%, respectively.[6,23] Clinical evaluation does not include the analysis of the respiratory mechanics, ventilatory demand, or respiratory muscle strength, which are important criteria, especially when evaluated in combination. The weaning indices inform decisions regarding MV weaning in patients at high risk for weaning failure.[7] Although a given index might not be very accurate overall, it is, in general, highly accurate when its values are extremely unfavorable (e.g., MIP > −15 or −10 cmH_2O). The indices are also useful in guiding the evaluation and treatment of patients in whom weaning from MV failed, identifying the causes of intolerance.[7] Even if the completion of the SBT is able to predict 85% of the chance of weaning success,[6] approximately 15% of patients do not tolerate the 48 h following extubation. In one study,[24] extubation failed in 121 (13.4%) of the 900 patients who completed the SBT. The clinical criteria to determine whether patients are ready to be weaned from MV are described in Chart 2.

Chart 2 - Clinical criteria that patients should meet in order to be considered ready for weaning from mechanical ventilation.

Clinical criteria for weaning from mechanical ventilation
Resolution or improvement of the condition that led to mechanical ventilation initiation
Patient without hypersecretion (defined as the need for aspiration > 2 h)
Effective cough (PEF > 160 L/min)
Hemoglobin > 8-10 g/dL
Adequate oxygenation (PaO_2/FiO_2 > 150 mmHg or SaO_2 > 90% and FiO_2 < 0.5)
Body temperature < 38.5-39.0°C
Without dependence on sedatives
Without dependence on vasopressor agents (e.g., dopamine < 5 µg • kg^{-1} • min^{-1})
No acidosis (pH ranging from 7.35 and 7.45)
No electrolyte disturbances
Adequate fluid balance

Predictive parameters for MV weaning

Among the various indices, the most well-known and most widely used is the rapid shallow breathing index, also known as the RR/V_T ratio.[25,26] The RR/V_T ratio has been evaluated in more than 22 studies,[26] having been mentioned and recommended in large-scale review articles on MV weaning.[1,8,9] There have been few original or review articles on MV weaning that did not consider the RR/V_T ratio. The RR/V_T ratio identifies the development of rapid shallow breathing. Although some studies have found the RR/V_T ratio to be inaccurate,[13,27,28] high RR/V_T ratios (> 100-105 breaths • min^{-1} • L^{-1}) are associated with unsuccessful weaning from MV.[1,8,9,16,25] The RR/V_T ratio was originally devised to be measured during spontaneous breathing, through the use of a spirometer connected to the artificial airway.[25] However, there have been studies evaluating the RR/V_T ratio on PSV and during CPAP.[16,27] The measurement of the RR/V_T ratio during CPAP at 5 cmH_2O yielded a result that was 28-38% lower than was that obtained during spirometry.[16] The measurement of the RR/V_T ratio on PSV at 10 cmH_2O yielded a result that was 46-82% lower than was that obtained through spirometry.[16] Therefore, the RR/V_T ratio should be measured during spontaneous breathing, through a spirometer, in order to maintain its cut-off value, typically between 100 and 105 breaths • min^{-1} • L^{-1}. If the RR/V_T ratio is measured during CPAP or on PSV, a different cut-off value should be validated, which has yet to be done.

According to review articles published as of 2009,[7,8,10] the principal parameters are as follows: the RR/V_T ratio; MIP; the airway occlusion pressure at 0.1 s ($P_{0.1}$)/MIP ratio; RR; V_T; minute volume; and an integrated evaluation of dynamic compliance, RR, oxygenation, and MIP, known as the compliance, rate, oxygenation, and pressure (CROP) index. Other important parameters include $P_{0.1}$,[11,17,19] $P_{0.1}$ × the RR/V_T ratio,[17] static respiratory system compliance (Cst,rs),[25,29] the PaO_2/FiO_2 ratio,[30,31] and VC.[13]

One group of authors recently devised a new index, designated the integrative weaning index

(IWI), which is calculated with the following formula[18]:

$$IWI = (Cst,rs \times SaO_2) \div RR/V_T \ ratio$$

The IWI is used in order to evaluate, in an integrative manner, respiratory mechanics, oxygenation, and breathing pattern. Since Cst,rs and SaO_2 are directly proportional to one another and indirectly proportional to the RR/V_T ratio, a higher IWI translates to a better prognosis. The measurement of Cst,rs during weaning was considered to be one of the limitations of that study.[18] Values of IWI ≥ 25 are predictive of successful weaning from MV.[18] On the basis of the scale proposed by Swets,[20] the IWI was shown to be highly accurate.[18] In the most recent analysis of the IWI, Nemer et al. prospectively evaluated 216 patients and found that the AUC for the IWI was greater than was that obtained for the RR/V_T ratio (0.96 vs. 0.85; p = 0.003), as well as being greater than the AUCs obtained for the other indices evaluated (p < 0.002).[18] Among the 216 patients, MV weaning failed in 33. Extubation failure occurred in 6 (18%) of the 33 patients who completed the SBT. The IWI was accurate in establishing a prognosis for 5 of the 6 patients. As in the study conducted by Frutos-Vivar et al.,[24] Nemer et al.

Chart 3 - Weaning indices, with the respective cut-off values, evaluated in the literature.

Indices	Author, year of publication	LR	AUC
RR/V_T < 105 breaths • min^{-1} • L^{-1}	Yang & Tobin, 1991[25]	NR	0.89
RR/V_T < 60 breaths • min^{-1} • L^{-1}	Capdevilla et al., 1995[19]	NR	0.72
RR/V_T < 100 breaths • min^{-1} • L^{-1}	Sassoon & Mahutte, 1993[17]	NR	0.78
RR/V_T < 100 breaths • min^{-1} • L^{-1}	Conti et al., 2004[13]	0.69	0.70
RR/V_T < 105 breaths • min^{-1} • L^{-1}	Nemer et al., 2009[18]	2.99	0.85
$P_{0.1}$ < 5.5 cmH_2O	Sassoon & Mahutte, 1993[17]	NR	0.64
$P_{0.1}$ < 5.0 cmH_2O	Capdevilla et al., 1995[19	NR	0.93
$P_{0.1}$ < 4.0 cmH_2O	Conti et al., 2004[13]	1.17	0.47
$P_{0.1}$ < 3.1 cmH_2O	Nemer et al., 2009[18]	2.52	0.73
MIP < −15 cmH_2O	Yang & Tobin, 1991[25]	NR	0.61
MIP < −50 cmH_2O	Capdevilla et al., 1995[19	NR	0.71
MIP < −16 cmH_2O	Conti et al., 2004[13]	0.87	0.57
MIP < −25 cmH_2O	Nemer et al., 2009[22]	NR	0.52
$P_{0.1}$/MIP < 0.09 cmH_2O	Capdevilla et al., 1995[19	NR	0.99
$P_{0.1}$/MIP < 0.15 cmH_2O	Conti et al., 2004[13]	1.87	0.71
$P_{0.1}$/MIP < 0.14 cmH_2O	Nemer et al., 2009[22]	NR	0.78
$P_{0.1} \times RR/V_T$ < 300 cmH_2O/breaths • min^{-1} • L^{-1}	Conti et al., 2004[13]	0.61	0.67
$P_{0.1} \times RR/V_T$ < 270 cmH_2O/breaths • min^{-1} • L^{-1}	Nemer et al., 2009[18]	2.81	0.81
$P_{0.1} \times RR/V_T$ < 450 cmH_2O/breaths • min^{-1} • L^{-1}	Sassoon & Mahutte, 1993[17]	NR	0.80
Cst,rs > 33 mL/cmH_2O	Yang & Tobin, 1991[25]	NR	0.68
Cst,rs > 30 mL/cmH_2O	Nemer et al., 2009[18]	3.40	0.83
RR < 38 breaths/min	Yang & Tobin, 1991[25]	NR	0.76
RR < 35 breaths/min	Conti et al., 2004[13]	1.17	0.52
RR < 30 breaths/min	Nemer et al., 2009[18]	1.87	0.76
Minute volume < 12 L	Conti et al., 2004[13]	1.0	0.54
Minute volume < 15 L	Yang & Tobin, 1991[25]	NR	0.76
PaO_2/FiO_2	Nemer et al., 2009[18]	1.79	0.65
IWI > 25 mL • cmH_2O^{-1} • breaths^{-1} • min^{-1} • L^{-1}	Nemer et al., 2009[18]	16.05	0.96
CROP > 13 mL • breaths^{-1} • min^{-1}	Yang & Tobin, 1991[25]	NR	0.78
VC > 11 mL/kg	Conti et al., 2004[13]	1.3	0.71
V_T > 5 mL/kg	Conti et al., 2004[13]	1.54	0.67
V_T > 315 mL	Nemer et al., 2009[18]	2.81	0.81

V_T: tidal volume; $P_{0.1}$: airway occlusion pressure; Cst,rs: static respiratory system compliance; IWI: integrative weaning index; CROP: compliance, rate, oxygenation, and pressure ([index] of dynamic compliance, respiratory rate, oxygenation, and MIP); LR: likelihood ratio; AUC: area under the (ROC) curve; and NR: not reported.

showed that the SBT is not always sufficient to evaluate the prognosis of weaning from MV and that the evaluation of certain weaning indices is therefore necessary.[18] Although the IWI has yielded promising results, the index must be tested in other studies in order to confirm its accuracy. Chart 3 shows the cut-off values that indicate successful weaning from MV, as well as the AUCs and the probabilities, for the IWI and other major international parameters.

Although it is widely used, MIP generally presents an inaccurate or moderately accurate AUC,[13,19,25] the values of which range from 0.57 to 0.71. Good respiratory muscle strength alone is not sufficient for patients to be weaned from MV, since the respiratory muscles are predominantly resistant muscles. However, MIP remains a valuable parameter, because patients who present with extreme inspiratory muscle weakness (MIP > −15 cmH_2O) will probably be unable to breathe spontaneously.

Another problem related to MIP is the wide range of methods for its measurement.[32] An analogical or digital vacuum manometer can be used in order to measure MIP. In addition, MIP can be measured with the software that accompanies artificial ventilators. Such software generally measures MIP without exhalation, a measurement that is consistent with that made by using a vacuum manometer without a unidirectional valve. When a unidirectional valve is used, patients can inhale and exhale deeply, reaching the inspiratory and expiratory reserve volumes, thereby generating greater force due to increased diaphragmatic mobility. When a unidirectional valve is not used, MIP is measured during V_T breathing, which generates less force due to decreased diaphragmatic mobility. Although MIP was originally intended to be measured with a unidirectional valve for 20 s,[16] there have been studies showing no differences between MIP measurements obtained with and without a unidirectional valve,[22] and measurement periods of longer than 20 s have been used.[32] The period during which MIP is measured varies greatly, ranging from 1 s to over 20 s.[32] Despite its name, MIP is, in some hospitals, still considered to be the mean of the values obtained with three or more measurements.[32] Although the most widely used method for measuring MIP is with a vacuum manometer coupled to a unidirectional valve, there is no consensus regarding the ideal method. In normal individuals, MIP is generally < −80 cmH_2O.[33] Values of MIP < −20 cmH_2O are predictive of successful weaning from MV.[16]

One important parameter for MV weaning from MV is $P_{0.1}$, which indicates central respiratory activity; however, in order to determine $P_{0.1}$, an esophageal balloon or ventilators should be introduced (tracheal $P_{0.1}$ is also considered to be an accurate MV weaning parameter).[33] Among the parameters that evaluate central respiratory activity, tracheal $P_{0.1}$ determination is probably the method that is most widely available in ICUs. The physiological values of $P_{0.1}$ range from 0.5 to 1.5 cmH_2O,[33] and $P_{0.1}$ values lower than 4.0[13] or 4.2 cmH_2O[16] generally predict successful weaning from MV. The AUC for $P_{0.1}$ generally ranges from 0.47[13] to 0.93.[19] In patients with certain conditions, including lung hyperinflation and reduced inspiratory muscle strength of various etiologies, it is rare to see an elevated $P_{0.1}$.[33] Therefore, although patients with neurological and neuromuscular diseases, as well as those with COPD, might present with increased central respiratory activity, their $P_{0.1}$ values might not be high. In addition, $P_{0.1}$ correlates with respiratory effort (a criterion that is also used to evaluate the prognosis for MV weaning): a $P_{0.1}$ value = 3.5 cmH_2O corresponds to a respiratory effort of approximately 0.75 J/L. Respiratory effort values lower than 0.75 J/L are considered predictive of successful weaning from MV.[33] Respiratory effort is automatically calculated and monitored by certain modern ventilators (those with microprocessors).

The $P_{0.1}$/MIP ratio is an integrative index that aims at increasing the accuracy of its two components. In one study,[19] the AUC for the $P_{0.1}$/MIP ratio (0.99 ± 0.01) was greater than was that that obtained for any of the other weaning indices evaluated. However, these results differ from those of other studies, in which the AUC for the $P_{0.1}$/MIP ratio ranged from 0.71[13] to 0.78.[22] In another study,[22] no significant differences were found between the AUC for $P_{0.1}$ and that for the $P_{0.1}$/MIP ratio (0.76 ± 0.06 vs. 0.78 ± 0.06; p = 0.69). However, the AUC for $P_{0.1}$ and that for the $P_{0.1}$/MIP ratio were both greater than was that for MIP in isolation (0.76 ± 0.06 vs. 0.52 ± 0.08; p = 0.004; and 0.78 ± 0.06 vs. 0.52 ± 0.08; p = 0.0006, respectively).[22] These results showed that only MIP was potentiated by the integration between $P_{0.1}$ and MIP, given that the AUC for $P_{0.1}$ and that for the $P_{0.1}$/MIP ratio were similar.[22]

The PaO_2/FiO_2 ratio, which is the reference for the evaluation of oxygenation in patients with acute lung injury and acute respiratory distress syndrome,[34] is not highly accurate for weaning from MV,[30,35] and the PaO_2/FiO_2 ratio cut-off values that predict successful weaning from MV vary greatly (from 150 to 200).[9] In one study,[30] 89% of the patients with a PaO_2/FiO_2 ratio of 120-200 were successfully extubated. In another,[35] a PaO_2/FiO_2 ratio of 238 showed a PPV of 90% but a NPV of 10%. Therefore, although the PaO_2/FiO_2 ratio is greatly valued, there are no justifiable reasons for its routine use as a parameter for MV weaning.

Although the PaO_2/FiO_2 ratio should remain as a reference for the evaluation of patients with acute respiratory distress syndrome and acute lung injury, it is not always an appropriate parameter for weaning from MV.

Of the more than 66 weaning indices proposed, only 5-7[7,10] are associated with significant clinical changes in the probability of the MV weaning outcome[7] or present a significant LR for the evaluation of MV weaning outcome.[10] Therefore, as of 2009, only the following weaning indices had been recommended for routine use: the RR/V_T ratio; MIP; the $P_{0.1}$/MIP ratio; RR; V_T; minute volume; and the CROP index. There is a wide divergence of opinion regarding the recommendations for routine use of the weaning indices. According to the leading specialist in this topic, Martin Tobin,[15,16,25,26] at least some of the indices, particularly the RR/V_T ratio, should be used routinely. However, according to another specialist, Scott Epstein, there have been two consensuses in which the routine use of weaning indices was not recommended.[36] Epstein recently questioned whether those recommendations might change if the accuracy of the IWI is confirmed.[36]

Pathophysiology of weaning failure and of extubation failure

Although weaning from MV depends on various factors, the principal factors are respiratory muscle strength, respiratory muscle load, and the intensity of the respiratory drive.[1] Generally, weaning from MV fails due to an imbalance between respiratory muscle function and the respiratory muscle load.[1,37] The causes of reduced respiratory muscle efficiency include central inhibition, bone marrow diseases, phrenic nerve injury, neuropathies, neuromuscular junction impairment, and muscle weakness of various etiologies.[8,37] The causes of increased ventilatory demand include increased central respiratory drive, sepsis, fever, pain, increased dead space ventilation, and decreased elastic recoil (of the lung and chest wall).[8,37]

The principal causes of MV dependence include neurological causes (due to respiratory system involvement or cardiovascular involvement) and psychological factors.[1,8,10] Other causes include metabolic disorders, endocrine dysfunction, electrolyte disturbances, malnutrition, obesity, and anemia.[8]

It is essential to identify the cause of MV weaning failure, in order to adopt a new approach that focuses on the triggering factor. Chart 4 shows the criteria for defining weaning failure.

Because weaning failure has various causes, integrative indices are generally more accurate.[10,18,25] The evaluation of the weaning indices aids in identifying the causative factor of MV weaning failure, which can then be treated.[7]

The etiology of extubation failure differs from that of weaning failure and is associated with upper airway impairment, including laryngospasm, abundant secretion, and ineffective cough.[1,11,14,30] Therefore, the accuracy of weaning indices in predicting extubation failure is limited.[14] Tests to evaluate extubation, such as the cuff leak test (which evaluates

Chart 4 - Criteria to define weaning failure.

Signs of intolerance to spontaneous breathing (weaning failure)
PaO_2 < 50-60 mmHg and FiO_2 > 0.5
SaO_2 < 88-90% and FiO_2 > 0.5
$PaCO_2$ > 50 mmHg or increased by more than 8 mmHg
pH < 7.32 or reduced by more than 0.07
RR > 35 breaths/min or increased by more than 50%
HR > 140 bpm or increased by more than 20%
SBP > 180 mmHg or < 90 mmHg
Uncontrollable psychomotor agitation
Reduced level of consciousness
Excessive sweating and cyanosis
Evidence of increased respiratory muscle effort

SBP: systolic blood pressure. Adapted from Boles et al.[8]

air leak after cuff deflation) are generally not recommended for routine use.[10,11] Extubation failure is associated with prolonged MV, with prolonged hospital stay, and with greater mortality, especially if reintubation is delayed.[1,14]

As previously mentioned, weaning failure is defined as intolerance to the SBT in the absence of ventilatory support, whereas extubation failure is defined as intolerance to extubation.[14] However, a diagnosis of extubation failure requires evidence of upper airway involvement (revealing orotracheal tube dependence).[10,14] In this aspect, this definition might not be precise, given that approximately 15% of patients tolerate the SBT but need to be reintubated,[6] not necessarily due to orotracheal tube dependence. Patients who require reintubation for reasons unrelated to the upper airways should not be classified as cases of extubation failure. Some patients tolerate the SBT for 2 h and are extubated without complications, only to subsequently develop respiratory failure without any type of impairment related to orotracheal tube dependence. Such patients should not be classified as cases of extubation failure, since the etiology is unrelated to orotracheal tube dependence. If the definition of extubation failure were applied to all reintubated patients, such patients would have to be classified as cases of extubation failure rather than weaning failure, as they are commonly diagnosed. We hope that the definition of extubation failure will one day be applied exclusively to cases of orotracheal tube dependence rather than to all reintubated patients.

Applications and limitations of the weaning indices in different populations

The weaning indices have some limitations, and it seems that the greatest of all is the wide variety of methods for their measurement. Such methods vary from hospital to hospital, as well as from professional to professional within the same hospital.[32] This variation can lead to great differences among the results obtained. There are over ten different types of MIP measurements, which depend on various factors, including the equipment used, the duration of occlusion, and the value used (the mean, the most negative value, or the most reproducible value).[32] The RR/V_T ratio should be measured during spontaneous breathing.[25] However, studies have measured the RR/V_T ratio during CPAP and even on PSV[16,27] without necessarily changing the cut-off value used, a fact that completely changes the results and prognoses of the parameter.[16]

Another major limitation is the fact that different cut-off values are used for different populations or even for similar populations. Although the original cut-off value for the RR/V_T ratio is 100-105 breaths • min^{-1} • L^{-1}, studies using cut-off values of 60 and 76 breaths • min^{-1} • L^{-1} have achieved greater accuracy than that achieved with the original cut-off value.[19,38]

The use of predictive indices in neurological patients does not seem to predict extubation outcome accurately.[39] In a retrospective analysis of 62 neurological patients,[39] traditional indices, such as the RR/V_T ratio, MIP, and the PaO_2/FiO_2 ratio, were found to have low sensitivity, low specificity, or both. In that study,[39] the RR/V_T ratio showed high specificity but low sensitivity (0.88 and 0.18, respectively). Not even the SBT was shown to be accurate in the study population, showing high sensitivity but low specificity (0.90 and 0.20, respectively).[39] In neurological patients, a Glasgow coma scale score ≥ 8 seems to be more accurate than are the traditional indices in predicting the outcome of weaning from MV.[40,41]

Studies evaluating weaning indices in patients with COPD have shown that the RR/V_T ratio[42] and $P_{0.1}$[43] are capable of identify weaning failure. Regarding the cut-off values used, one group of authors[44] showed that the cut-off values for COPD patients are generally different from (10% higher than) those used for heterogeneous populations. That study[44] revealed that the AUCs for the indices evaluated (MIP, RR/V_T ratio, Cst,rs, RR, the CROP index, and $P_{0.1}$/MIP ratio) were greater than the 0.9 only for the CROP index and for $P_{0.1}$. One group of authors[45] recently evaluated 64 patients with COPD and reported that the RR/V_T ratio was inaccurate in predicting MV weaning outcome, despite the fact that two cut-off values were used: the traditional cut-off value of 105 breaths • min^{-1} • L^{-1} and a higher cut-off value, of 130 breaths • min^{-1} • L^{-1}. For the cut-off value of 105 breaths • min^{-1} • L^{-1}, the specificity and sensitivity of the RR/V_T ratio were only 0.38 and 0.63, respectively, compared with 0.66 and 0.54, respectively, for the cut-off value of 130 breaths • min^{-1} • L^{-1}. The evaluation of the weaning indices in patients with COPD has been shown to be only moderately accurate,[12] and there seems to be no gold standard index for that population.[44]

Weaning indices have also been evaluated in patients on MV for prolonged periods.[31,46,47] One group of authors[31] retrospectively evaluated clinical criteria and certain weaning indices in 1,307 patients in whom MV was prolonged. Of the weaning indices evaluated (the PaO_2/FiO_2 ratio, the RR/V_T ratio, and MIP), only the RR/V_T ratio identified no statistically significant differences between patients who had been weaned from MV and those who had not (146.4 ± 91.4 vs. 154.5 ± 106.2 breaths • min^{-1} • L^{-1}; p = 0.262).[31] Another group of authors[47] evaluated various weaning indices in 30 patients in whom MV was prolonged. Of the traditional weaning indices/criteria evaluated (V_T, the RR/V_T ratio, dynamic compliance of the respiratory system, and MIP), only the RR/V_T ratio and MIP identified statistically significant differences between patients who had been weaned from MV and those who had not (74.1 ± 44.0 vs. 148.2 ± 121.4 breaths • min^{-1} • L^{-1}; p = 0.03; and 57.3 ± 18.2 vs. 38.6 ± 13.5 cmH_2O; p = 0.001, respectively). Because controlled MV directly affects the diameter of diaphragm muscle fibers types I and II, reducing it by more than 50% over periods longer than 18 h of continuous MV, weaning indices that evaluate diaphragm strength, such as MIP, might be successfully applied to that population.[4,48]

There is evidence that the use of weaning protocols are associated with decreases in duration of MV, length of hospital stay, and weaning time.[49] The predictive parameters for weaning are included in weaning protocols,[8-10,49] which greatly improve the results of these protocols.

Final considerations

The weaning indices have limitations, which are principally related to the study population, the cut-off values used, and the means of measurement. Although the weaning indices can be used in homogeneous populations, the accuracy of the indices might be lower in such populations than in heterogeneous populations. The evaluation of weaning indices in neurological patients seems to be the least indicated among those related to homogeneous populations.

Although integrative indices are generally more accurate, their accuracy in predicting the outcome of extubation might be limited.

Since the accuracy of the SBT in evaluating the prognosis of weaning from MV is approximately 85% and clinical evaluation alone is not sufficient, accurate indices, such as the RR/V_T ratio and the recently devised IWI, might be needed in order to make the outcome of weaning from MV safer.

The weaning indices are useful in identifying patients who will probably be unable to tolerate weaning from MV. The weaning indices are also useful in identifying reversible causes of weaning failure, serving as references for subsequent attempts.

Although few of the weaning indices are accurate, we are of the opinion that at least 5 of these indices should be recommended for routine use. Because the clinical impression and SBT are not 100% accurate, the MV weaning parameters can be useful, especially in situations in which the decision to wean from MV is problematic.

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